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Is COVID-19 a risk for postoperative delirium and death in elderly patients after emergency surgery?

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Abstract

Aim: While recent evidence describes atypical outcomes of coronavirus disease 2019 (COVID-19) in elderly patients, the frequency of delirium and associated outcomes in elderly patients with COVID-19 (coronavirus disease 2019) infection undergoing emergency surgery are not well defined. This study aims to determine the effect of COVID-19 on postoperative delirium and postoperative death in elderly patients undergoing emergency surgery.

Material and Methods: This descriptive and cross-sectional study was conducted in general surgery, orthopedics, and cardiovascular surgery clinics of a public hospital, including 30 days of follow-up between April 1 and May 1, 2021. All patients who were admitted to these clinics for emergency surgery intervention on these dates constituted the study population, while a total of 140 patients aged ≥65 years, who met the study criteria, formed the sample of the study. Descriptive Characteristics Form and Nursing Delirium Screening Scale (Nu-DESC) were used as data collection tools in the study. SPSS 25.0 statistical program was used for data analysis.

Results: Thirty (42.85%) of the SARS-CoV-2 positive (n=70) patients developed delirium in the study. 12.9% (n=18) of the patients died within 30 days of follow-up after surgery. There were 30 (69.8) of 70 SARS-CoV-2 positive patients who developed delirium, and 12 patients (25.5) died after testing positive for COVID-19, with a mean of 8.08∓1.56 days within 30 days of admission.

Discussion: These findings may lead to a poor clinical prognosis for COVID-19 infection delirium and postoperative death in patients over 65 years of age undergoing emergency surgery.

Keywords

COVID-19 Pandemic, Postoperative Delirium, Old Age, Risk Factors

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Introduction

While the most common and life-threatening complication of coronavirus disease 2019 (COVID-19) is a respiratory complication, there are increasing reports of neurological and psychiatric involvement [1]. Delirium may be a symptom of many diseases, especially in frail and elderly patients, and is considered an independent risk factor for mortality [2]. The overall prevalence of delirium in the hospital setting is approximately 14-24%; it is approximately 30% higher in emergency room surgeries or medical services [3]. To date, clinical manifestations of delirium in elderly patients with COVID-19 have rarely been described; however, few studies have analyzed the clinical aspects of delirium in COVID-19. Some studies have focused on epidemiological data and outcomes [4]. Delirium is one of the most common neurological disorders, and if it is not recognized and treated when surgical intervention is required, it increases morbidity and mortality [5]. COVID-19 contributes to delirium through several brain pathways [6]. Significant contributors include cytokine storms and immune dysregulation accompanying COVID-19, which trigger neuroinflammation (in the brain and meninges) and hypercoagulability. The hypercoagulable state contributes to cerebral infarction in 1% to 3% of hospitalized patients with COVID-19, more often from large than small-vessel involvement [7]. This study involving 214 patients diagnosed with COVID-19 showed that 45% of conscious patients had neurological symptoms, and some of them had some symptoms indicating impaired consciousness [8]. In patients with COVID-19, delirium may develop due to factors such as direct central nervous system (CNS) involvement, induction of CNS inflammatory mediators, the secondary effect of other organ system failure, the effect of sedative strategies, prolonged mechanical ventilation time, or social isolation [6]. Notably, delirium occurring during COVID-19 may also be a sign of prodromal infection or hypoxia associated with severe respiratory failure [9]. Acute infections, respiratory diseases, pneumonia, acute lung disease, and surgical interventions are factors that cause delirium in the elderly, and cognitive changes may develop in these patients. Delirium after surgical intervention is an independent predictor of higher mortality, higher treatment costs, and more extended treatment and hospitalization [10]. After surgical intervention, the systemic inflammatory process is activated leading to the release of cytokines and neurotransmitters. Cytokines initiate microglial activation, increasing the permeability of the blood-brain barrier to neurotoxins and leading to cognitive impairment [11].

Understanding the epidemiological features of delirium and COVID-19 is an urgent research priority, especially in older people, where age increases the risk of developing delirium and COVID-19-related death. Recently, the volume of published literature on delirium in patients with COVID-19 has increased. Therefore, a comprehensive synthesis of existing evidence investigating the prevalence, incidence, and mortality of delirium in COVID-19 patients is necessary to inform clinical care and public health policies. In this study, we aimed to identify mortality differences between COVID-19 patients with and without delirium.

Material and Methods

This study was initiated after obtaining permission from the Ethics Committee of a Foundation University (Decision no:11-01-2021/E-20292139-050.01.04-424) and the head physician of the public hospital, where the research was conducted in terms of the feasibility of the research. This descriptive study was conducted at the Orthopedics, Cardiovascular, and General Surgery Clinics of a Public Hospital in Istanbul between April and May 2021. In this study, patients were evaluated for delirium for an average of 3 days after emergency surgery. In this study, patients who continued to be treated in the hospital for at least seven days after surgical intervention were evaluated for delirium for three days. The study population consisted of patients aged ≥ 65 years who were hospitalized for emergency surgical intervention at the institution where the study was conducted, who voluntarily agreed to participate in the study, and whose verbal and written consent was obtained. While some of these patients had a positive preoperative COVID-19 test, others had a positive post-intervention COVID-19 test. This study included 140 patients who met the inclusion criteria without selecting a sample. To eliminate the effect of confounding factors, 70 patients over 65 years of age who underwent emergency surgery and had a negative test were included in the study as the control group, and 70 patients with a positive test (Figure 1). Four patients were excluded from the study because they were transferred to the preoperative intensive care unit due to respiratory problems.

In this study, the "Descriptive Characteristics Form" and "Nursing Delirium Screening Scale (Nu-DESC)" were used as data collection tools. The Nursing Delirium Screening Scale (NU-DESC) was used to screen for post-surgical delirium. This scale was described by Gaudreau et al. (2005) and consists of five items: disorientation, inappropriate behavior, inappropriate communication, illusion-hallucination, and psychomotor slowing [12]. Patients were identified as COVID-19 positive if presented positive swab test confirming SARS-CoV-2 infection. To determine post-surgical delirium, the "Nurse Delirium Screening Scale" was performed 1-3 days after surgery, and delirium screening was performed three times a day between 08-16, 16-24, 24-08 hours. According to the symptoms appearing at these time intervals, a neurologist's consultation was requested to diagnose delirium, which was recorded. Clinical physicians and nurses were informed about the initiation of necessary interventions for patients diagnosed with delirium. Delirium was indicated by a total of ≥2 points.

Data analysis

The data were analyzed using the Statistical Package for Social Sciences version 25.0 software for Windows. The Kolmogorov-Smirnov and Shapiro-Wilk tests, Fisher's precision test, the Mann-Whitney-U test, and Student's t-test for independent groups were used in the analysis. The Kaplan-Meier analysis was used to calculate the probability of survival. Statistical significance was set at $p \leq 0.001$ and $p \leq 0.05$, respectively.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

A total of 140 patients, 84 (60 %) men and 56 (40 %) women were included in the study. While delirium developed in 33.6% of the patients (n=47), it did not develop in 66.4% (n=93). Thirty (42.85%) of the SARS-CoV-2-positive (n=70) patients developed delirium. There were 140 patients who got tested, and 70 (50%) were positive for SARS-CoV-2 and 13 (5 9.3) of these patients were positive before surgery. They died within 30 days of follow-up after surgery, which accounted for 12.85% of the patients (n=18). There were 30 (69.8%) of 70 SARS-CoV-2-positive patients who developed delirium, and 12 patients (25.5%) died after testing positive for COVID-19, with a mean of 8.08∓1.56 days within 30 days of admission. Peri-operative risk factors were compared according to the development of delirium in the patients included in the study (Table 1). There was a significant difference ($p<0.05$) between patients with and without delirium. Baseline characteristics and comparison of perioperative risk factors in COVID-19 patients with and without delirium are presented in Table 1.

There was a significant difference ($p<0.05$) between patients with and without delirium. Comparison of perioperative risk factors in COVID-19 patients with and without delirium is presented in Table 2.

The results of the logistic regression analysis are presented in Table 3.

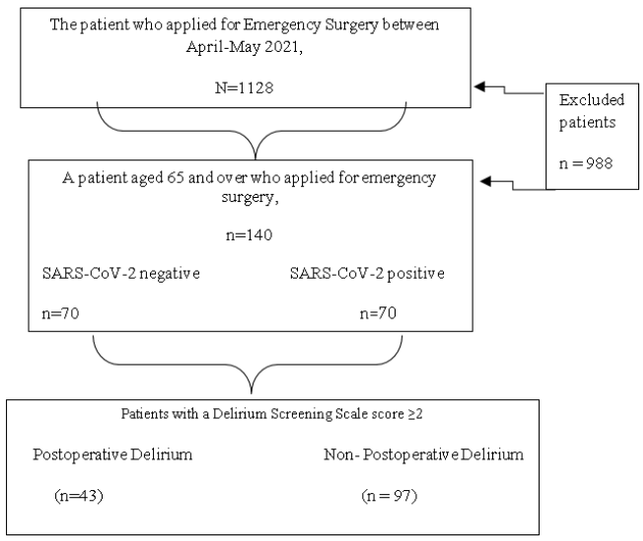

Figure 1. (Research) Flow Diagram

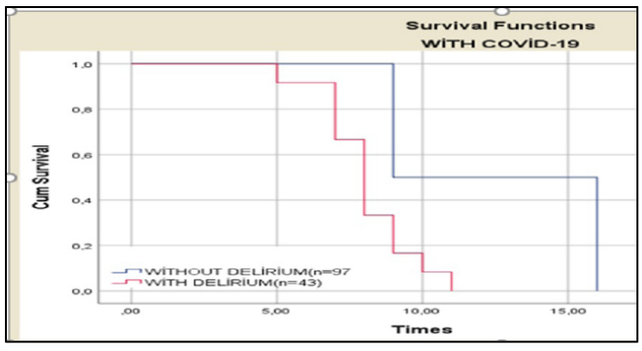

Figure 2. Analysis of survival among patients with COVID-19 with and without delirium.

Table 1. Baseline characteristics and Comparison of perioperative risk factors in COVID-19 patients with and without delirium.

Demographic	Category	Non-Delirium n=97	Delirium n=43	p-value
Sex	(F/M)	35 (36.1)	13 (30.2)	0.566
		62 (63.9)	30 (69.8)	
Chronic Disease	No	44 (45.4)	13 (30.2)	0.098
	Yes	53 (54.6)	30 (69.8)	
Hypertension, n (%)	No	39 (40.2)	13 (30.2)	0.343
	Yes	58 (59.8)	30 (69.8)	
DM, n (%) [1]	No	46 (47.4)	13 (30.2)	0.065
	Yes	51 (52.6)	30 (69.8)	
CAD [2]/HF, n (%)	No	54 (55.7)	15 (34.9)	0.028
	Yes	43 (44.3)	28 (65.1)	
CVD, n (%)	No	70 (72.2)	13 (30.2)	0.000
	Yes	27 (27.8)	30 (69.8)	
Respiratory disease, n (%)	No	74 (76.3)	17 (39.5)	0.000
	Yes	23 (23.7)	26 (60.5)	
Multiple Drug Use	1-3,	21 (21.6)	5 (11.6)	0.000
	4-6,	62 (63.9)	10 (23.3)	
	7 ≥	14 (14.4)	28 (65.1)	
Defect of Vision	No	72 (74.2)	25 (25.8)	0.000
	Yes	16 (37.2)	27 (62.8)	
Number of Patients Taken to Intensive Care	No	28 (28.9)	4 (9.3)	0.015
	Yes	69 (71.1)	39 (36.1)	
Follow-Up				
Death	No	87 (93.5)	35 (74.5)	0.003
	Yes	6 (6.5)	12 (25.5)	
Blood Pressure	<130/80	27 (27.8)	24 (55.8)	0.002
	130/80	55 (56.7)	11 (25.6)	
	>130/80	15 (15.5)	8 (18.6)	
Blood Loss	<500ml	83 (85.6)	22 (51.2)	0.000
	500-1000	14 (14.4)	21 (48.8)	
Ventilator Support	Yes	84 (86.6)	0 (0.00)	0.000
	No	13 (13.4)	43 (100.0)	
Postoperative Nutrition	IV	56 (57.7)	22 (51.2)	0.580
	Oral	41 (42.3)	21 (48.8)	
COVID-19 status, n (%)	Negative	57 (58.8)	13 (30.2)	0.003
	Positive	40 (41.2)	30 (69.8)	

Pearson x^2 test for categorical variables. Significance was evaluated at the $p<0.05$ level, P=Fisher's Exact Test. [1]D.M., diabetes mellitus; [2]CAD/H.F., coronary artery disease/heart failure; CVD, cardiovascular disease.

A survival probability assessment in delirious and non-delirious COVID-19 patients was performed using the Kaplan-Meier curve (Figure 2). There was a statistically significant difference in the 30-day survival between the two groups, which was in favor of patients without delirium ($p <0.001$).

Discussion

In this study, 30 (69.8%) of the SARS-CoV-2 positive (n=70) patients developed delirium, and 12 (25.5%) of these patients developed death with a mean of 8.08±1.56 days within 30 days of admission. Patients who were SARS-CoV-2 positive before or after surgery and who developed delirium had a significantly lower survival rate than those without a proven infection. In addition, in COVID-19 patients, delirium was three times higher (95% CI: 1.52-7.07) when the patients were COVID-19 positive. Postoperative death was 4.9 times (95% CI: 1.73-14.28%)

Table 2. Comparison of perioperative risk factors in COVID-19 patients with and without delirium.

Demographic	Category	Non-Delirium n=97	Delirium n=43	p-value
Age (year),	Mean ∓ SD	76.19 ∓ 6.31	79.06.80 ± 6.71	0.019
Timing of death (until day 30)	(mean ± SD)	12.50 ∓ 2.8	8.08 ∓ 1.56	0.001
Time of stay in the ward (including the day of admission and discharge)	(mean ± SD)	7.18 ± 5.22	9.46 ± 8.10	0.054
Surgical Operation Time (min.)	(mean ± SD)	175.55 ∓ 55.62	196.51 ∓ 47.99	0.025
Anesthesia Duration	(mean ± SD)	175.58 ∓ 55.26	190.23 ∓ 61.54	0.182
Laboratory Data on Admission				
Hemoglobin, (%)	(mean ± SD)	11.9(7.7-14.1)	11.1(5.0-11.4)	0.056
Hematocrit, (%)	(mean ± SD)	32.7(24.2-39.6)	31.9(17.3-41.8)	0.113
Total protein, (g/dL)	(mean ± SD)	5.6(3.4-5.7)	5.8(4.1-6.7)	0.061
Albumin, (g/dL)	(mean ± SD)	3.0(2.0-4.1)	2.6(2.6-3.7)	0.003
BUN [4], (mg/ dL)	(mean ± SD)	20.0(7.0-66.0)	20.5(15.0-49.0)	0.128
C-reactive protein, (mg/L)	(mean ± SD)	56.0(1.0-218.0)	86.31(1.7-383.7)	0.021
IL-6	(mean ± SD)	51.21(24.6-181.47)	218.5(11.7-451.3)	0.017
Respiratory Parameters				
SpO2	(mean ± SD)	93.85 ± 3.56	94.16 ± 4.18	0.542
PO2 (mmHg)	(mean ± SD)	76.01 ± 18.09	71.83 ± 16.14	0.037
PCO2 (mmHg),	(mean ± SD)	34.35 ± 5.69	33.42 ± 5.57	0.126
FiO2	(mean ± SD)	0.37 ± 0.34	0.71 ± 0.38	0.000
PO2/FiO2	(mean ± SD)	262.13 ± 145.23	162.17 ± 129.12	0.000

Pearson's x^2 test for categorical variables. Significance was evaluated at the p<0.05 level, [4]BUN, blood urea nitrogen. FiO2—fraction of inspired oxygen, , n—number of patients, p—statistical significance, pCO2—partial pressure of carbon dioxide, pO2—partial pressure of oxygen, SD—standard deviation, SpO2— peripheral oxygen saturation.

Table 3. Risk factors for delirium determined by Univariate logistic regression analysis.

Predictors in model	Difference/OR (95% CI	p-value
Age	1.11 (0.085 to 4.34)	0.049
CAD [2]/HF, n (%)	2.33(1.11 to 4.93)	0.000
CVD, n (%)	5.98 (2.72 to 13.1)	0.004
Respiratory disease, n (%)	4.92(2.27 to 10.6)	0.003
Multiple Drug Use	1.01(0.793 to 1.026)	0.000
1-3;4-6;7 ≥		
Defect of Vision	4.86(2.25 to 10.4)	0.000
Number of Patients Taken to Intensive Care	3.92(1.29 to 12.11)	0.015
Death	4.97 (1.73 to 14.28)	0.003
Timing of death (until day 30)	3.52(1.32-12.74)	0.000
Blood Pressure	1.30(0.634-2.68)	0.002
Blood Loss	5.65(2.48-12.89)	0.000
Ventilator Support	4.30 (2.67-6.93)	0.000
Surgical Operation Time (min.)	9.24(2.68 to 39.23)	0.025
Albumin, (g/dL)		0.003
C-reactive protein, (mg/L)	4.31 (1.456 to 12.55)	0.011
IL-6	7.84 (2.89 to 23.58)	0.031
COVID-19 status, n (%)	3.28 (1.52 to 7.07)	0.002
Negative/Positive		
pO2 (mmHg)	4.59 (1.521 to 11.98)	0.000
FiO2	3.29 (1.582 to 12.38)	0.018
pO2/FiO2	1.72 (0.856 to 2.54)	0.000

Significance was evaluated at the p<0.05 level, CAD/H.F., coronary artery disease/heart failure; CVD, cardiovascular disease; FiO2—fraction of inspired oxygen, n—number of patients, p—statistical significance, pCO2—partial pressure of carbon dioxide, pO2—partial pressure of oxygen, SD—standard deviation, SpO2— peripheral oxygen saturation, IL-6 Interleukin 6, OR; Odds rate, CI; confidence interval.

higher than in those without delirium. In the meta-analysis study, the prevalence, incidence, and mortality from delirium in COVID-19 patients were 24.3% (95% CI: 19.4-29.6%), 32.4% (95% CI: 20.8-45.2%), and 44.5% (95% CI: 36.1-53.0%), respectively. In addition, mortality in COVID-19 patients with delirium increased 3-fold than in those without delirium [5]. Mounting evidence supports the high occurrence of delirium and other neuropsychiatric manifestations of COVID-19 [13,14]. A recent study reported delirium as a common presenting symptom in older adults without any other typical COVID 19 symptoms [15]. The literature supports the results of this study. In our study, in COVID-19 patients with delirium, mortality was 4.9 times higher than in those without delirium. The pathophysiology of this excess mortality in COVID-19 patients with delirium is likely to be multifactorial, but it is suggested that brain involvement in COVID-19, rather than worsening of pre-existing comorbidities, is responsible [16].

According to the results of multivariate logistic regression analysis, it was determined that delirium developed 3.2 times more in those with positive COVID-19 status, which was the starting point of the study, compared to those with negative COVID-19 status. The odds of mortality in COVID-19 patients presenting with delirium at any point of hospitalization was 17 times higher [17]. This study determined that chronic diseases were risk factors for the development of both COVID-19 and delirium and contribute to the development of delirium, which is consistent with the literature.

Older people usually also have other co-morbidities that induce chronic inflammatory states, such as hypertension, obesity, and diabetes mellitus, which contribute to the development of severe COVID-19 by activating RAS, which then activates the angiotensin II type 1 receptor and produces pro-inflammatory cytokines, vasoconstriction, fibrosis, thrombosis, and reactive oxygen species (ROS). Moreover, older patients have a reduced expression of ACE2 and therefore a reduced capacity to produce vasodilators, anti-inflammatory, anti-fibrosis, anti-thrombosis, and ROS neutralizer [18]. These conditions likely contribute to the development of poor outcomes from COVID-19 in older patients who present with delirium symptoms. It should also be noted that delirium occurring during COVID-19 may be a manifestation of a prodromal infection or hypoxia associated with severe respiratory failure [11]. The results of this study were similar to those reported in the literature.

Conclusion

In elderly patients undergoing emergency surgery for severe SARS-CoV-2 infection, delirium is an early sign of deterioration of homeostasis; therefore, it should be monitored and prevented to avoid increased mortality. Elderly people are the most vulnerable to severe COVID-19 infection and mortality rates. The current diagnostic guideline for COVID, does not routinely exclude delirium, leading to an under-detection of COVID-19. The addition of delirium as a common symptom of COVID-19 would avoid missing important cases and allow earlier identification and management of vulnerable patients

at a high risk for poor outcomes. Identifying risk factors in seeing, recognizing, and monitoring the process can guide preventive interventions. Therefore, it is recommended to focus on delirium-prone patients based on these risk factors when designing future delirium prevention strategies or etiological studies.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
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References
1. Leonardi M, Padovani A, McArthur JC. Neurological manifestations associated with COVID-19: a review and a call for action. J Neurol. 2020;267(6):1573-76.
2. Persico I, Cesari M, Morandi A. Frailty and Delirium in Older Adults: A Systematic Review and Meta-Analysis of the Literature. J Am Geriatr Soc. 2018;66(10):2022-30.
3. Morandi A, Di Santo SG, Zambon A, Mazzone A, Cherubini A, Mossello E, et al. Delirium, dementia, and in-hospital mortality: the results from the Italian Delirium Day 2016 a national multicenter study. The Journals of Gerontology: Series A. 2019; 74(6):910-16.
4. Alkeridy WA, Almaghlouth I, Alrashed R. A. Unique Presentation of Delirium in a Patient with Otherwise, Asymptomatic COVID-19. J Am Geriatr Soc.2020;68(7):1382-84.
5. Shao SC, Lai CC, Chen YH, Chen YC, Hung MJ, Liao SC. Prevalence, incidence and mortality of delirium in patients with COVID-19: a systematic review and meta-analysis. Age Ageing. 2021; 50(5):1445-53.
6. Kotfis K, Roberson SW, Wilson JE. COVID-19: ICU delirium management during SARS-CoV-2 pandemic. Crit Care. 2020;24(1):176.
7. Inouye SK. The Importance of Delirium and Delirium Prevention in Older Adults During Lockdowns. JAMA. 2021;325(17):1779-80.
8. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, Hu B. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol. 2020;77(6): 683-90.
9. Girard TD, Thompson JL, Pandharipande PP, Brummel NE, Jackson JC, Patel M. B, et al.
Clinical phenotypes of delirium during critical illness and severity of subsequent long-term cognitive impairment: a prospective cohort study. The Lancet Respiratory Medicine. 2018;6(3):213-22.
10. Ahmad I, Rathore FA. Neurological manifestations and complications of COVID-19: A literature review. JOCN. 2020;77: 8-12.
11. Hayhurst CJ, Patel MB, McNeil JB, Girard TD, Brummel NE, Thompson JL, et a. Association of neuronal repair biomarkers with delirium among survivors of critical illness. J Crit Care. 2020; 56: 94-99.
12. Çınar F, Aslan, FE. Evaluation of postoperative delirium: validity and reliability of the nursing delirium screening scale in the Turkish language. Dement Geriatr Cogn Disord Extra. 2019; 9(3):362-73.
13. Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, et al. Neurologic features in severe SARS-CoV-2 infection. New England Journal of Medicine. 2020;382(23): 2268-70.
14. Krewulak K D, Stelfox HT, Leigh J P, Ely EW, Fiest K M. Incidence and prevalence of delirium subtypes in an adult ICU: a systematic review and meta-analysis. Crit Care Med. 2018;46(12): 2029-35.
15. Kennedy M, Helfand BK, Gou RY, Gartaganis SL, Webb M, Moccia JM, et al. Delirium in older patients with COVID-19 presenting to the emergency department. 2020;2;3(11):e2029540.
16. Mcloughlin BC, Miles A, Webb TE, Knopp P, Eyres C, Fabbri A, et al. Functional and cognitive outcomes after COVID-19 delirium. Eur Geriatr Med. 2020; 11(5): 857-62.
17. Kotfis K, Witkiewicz W, Szylińska A, Witkiewicz K, Nalewajska M, Feret W, et al. Delirium Severely Worsens Outcome in Patients with COVID-19—A Retrospective Cohort Study from Temporary Critical Care Hospitals. J Clin Med. 2021;10(13): 2974.
18. Czick M, Shapter C, Shapter R. COVID's Razor: RAS Imbalance, the Common Denominator Across Disparate, Unexpected Aspects of COVID-19. Diabetes Metab Syndr Obes. 2020; 13: 3169.

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